BIOCHEMISTRY 640

(Biomembranes Discussion Group)

Wednesday, March 14, 2018

Room 4-70 Medical Sciences Building

4:00 PM

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"Intramembrane proteolysis modulates mitochondrial localization of STARD7"

Intramembrane proteolysis is a process by which proteases embedded within a lipid bilayer cleave transmembrane substrates to release signalling molecules. These proteolytic events are essential for numerous cellular processes including cell cycle signalling, proliferation, and apoptosis. The focus of this paper is the mitochondrial rhomboid protease, PARL, which has a defined role in maintaining mitochondrial homeostasis; the most well-characterized role of PARL in the mitochondria is its cleavage of the PINK1 protein which is a key factor in the mitophagy pathway. This paper presents a newly identified substrate of PARL, the lipid transfer protein STARD7, and defines a mechanism by which PARL is responsible for regulating the localization of this protein between the mitochondria and the cytosol. STARD7 has been found to localize to both the cytosol and the mitochondrial intermembrane space, which allows it to carry out its function of transferring phosphatidylcholine from the cytosol to the mitochondrial membranes. The factors that influence this partitioning, though, remain unclear. The results of this paper suggest that PARL-mediated cleavage of STARD7 occurring in a TIM23-dependent or independent manner, along with an internal sorting signal in the protein, allow mature STARD7 to have dual localization, with one fraction partitioning to the mitochondria and the other partitioning to the cytosol. Interestingly, several other substrates of PARL also have dual-localization characteristics, allowing the findings of this paper to be applied to other scenarios. This paper aids in our understanding of how PARL-mediated intramembrane proteolysis in the inner mitochondrial membrane has a critical role in modulating the localization of its substrates.

Reference:

Saita, S. *et al.* (2018). PARL partitions the lipid transfer protein STARD7 between the cytosol and mitochondria. *EMBOJ 37*(4). doi: 10.15252/embj.201797909